Safety of perioperative aspirin therapy in pancreatic operations

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Background. *Antiplatelet therapy with aspirin is prevalent among patients presenting for operative treatment of pancreatic disorders. Operative practice has called for the cessation of aspirin 7–10 days before elective procedures because of the perceived increased risk of procedure-related bleeding. Our practice at Thomas Jefferson University has been to continue aspirin therapy throughout the perioperative period in patients undergoing elective pancreatic surgery.*

Study design. *Records for patients undergoing pancreatoduodenectomy, distal pancreatectomy, or total pancreatectomy between October 2005 and February 2012 were queried for perioperative aspirin use in this institutional research board–approved retrospective study. Statistical analyses were performed with Stata software.*

Results. *During the study period, 1,017 patients underwent pancreatic resection, of whom 289 patients (28.4%) were maintained on aspirin through the morning of the operation. Patients in the aspirin group were older than those not taking aspirin (median 69 years vs 62 years, P < .0001). The estimated intraoperative blood loss was similar between the two groups, aspirin versus no aspirin (median 400 mL vs 400 mL, P = .661), as was the rate of blood transfusion anytime during the index admission (29% vs 26%, P = 0.37) and the postoperative duration of hospital stay (median 7 days vs 6 days, P = .103). The aspirin group had a slightly increased rate of cardiovascular complications (10.1% vs 7.0%, P = .107), likely reflecting their increased cardiovascular comorbidities that led to their physicians recommending aspirin therapy. Rates of pancreatic fistula (15.1% vs 13.5%, P = .490) and hospital readmissions were similar (16.9% vs 14.9%, P = .451).*

Conclusion. *This is the first study to report that aspirin therapy is not associated with increased rates of perioperative bleeding, transfusion requirement, or major procedure related complications after elective pancreatic surgery. These data suggest that continuation of aspirin is safe and that the continuation of aspirin should be considered acceptable and preferable, particularly in patients with perceived substantial medical need for treatment with antiplatelet therapy. (Surgery 2014;155:39-46.)*

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INTRODUCTION

Cardiovascular disease, including coronary artery disease (CAD), cerebrovascular disease (CVD), and peripheral vascular disease (PVD), is the leading cause of morbidity and mortality in the United States, accounting for 900,000 deaths per year.[1] The risk of cardiovascular disease is increased even more in diabetic patients.[2] The risk of perioperative cardiac events after major non-cardiac surgery ranges from 1.4% among the general population older than 50 years of age and increases up to 3.9% in those who are at risk of cardiac disease.[3] Aspirin decreases the risk of thrombotic events[4] and is the most widely prescribed antiplatelet agent in clinical practice. A randomized controlled trial showed an absolute risk reduction of 7.2% within 30 days of major noncardiac surgery when aspirin was continued.[5]

Aspirin inhibits platelet function and, thereby, has modest effects on hemostasis. It causes irreversible inhibition of cyclooxygenase-1 (COX-1),[6] which is necessary in the formation of prostaglandin. The prostaglandin metabolite thromboxane A_2 (TXA_2)

Presented as a Scientific Paper at the 98th Annual American College of Surgeons Clinical Congress, October 4, 2012, in Chicago, IL, and at the 47th annual meeting of the Pancreas Club, May 18, 2013, in Orlando, FL.

Accepted for publication May 28, 2013.

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0039-6060/$ - see front matter

http://dx.doi.org/10.1016/j.surg.2013.05.031

causes platelet shape change and aggregation,[7] and the lack of TXA_2 prevents platelets from having an active role in the formation of the platelet plug and vasoconstriction that leads to hemostasis. The full effect of COX inhibition on platelets is manifested just 30 minutes after the ingestion of aspirin[8] and lasts for the lifespan of the normal human platelet, 8–10 days. Other pathways for platelet activation and aggregation remain intact, making aspirin a relatively weak anticoagulant compared with adenosine diphosphate receptor and glycoprotein IIb/IIIa inhibitors[8] such as clopidogrel (Plavix) and eptifibatide (Integrilin), respectively.

The fear of excessive operation-related bleeding has led to a many decade-long general recommendation that antiplatelet agents including aspirin be discontinued 7–10 days preoperatively to avoid this complication. Research has shown that interruption in aspirin therapy may lead to an increase in thrombotic events during the period that the drug is being withheld. This concept is attributed to excessive TXA_2 activity and decreased fibrinolysis, the so-called "aspirin withdrawal syndrome."[9-13]

In this study we evaluated several perioperative parameters in patients undergoing major pancreatic procedures to determine whether the continuation of aspirin therapy throughout the perioperative period in this presumably greater-than-normal risk cardiac population increases the risk of procedure-related bleeding. We further analyzed differences in cardiac and noncardiac outcomes, recognizing that patients who had previously been placed on aspirin by their physicians were more likely to have an increased rate of cardiac comorbidities. Our hypothesis was that continuation of aspirin therapy would be the safest practice to minimize cardiovascular thrombotic events in patients and that it would not be associated with an increased risk of perioperative bleeding.

METHODS

Since October 2005 patients undergoing major elective pancreatic resection (pancreatoduodenectomy, distal pancreatectomy, or total pancreatectomy) at the Thomas Jefferson University Hospital (Philadelphia, PA) who were taking daily aspirin have been advised to continue aspirin therapy through the morning of the operation. This practice involved a concerted and intentional effort to change the previous routine practice of discontinuing aspirin preoperatively for patients undergoing operative procedures.

The senior surgeon in this study (C.J.Y.), as the Chair of the Department of Surgery, worked to alter the practices in the Patient Testing Center, educating those health care professionals on the merits of continuing aspirin as well as the potentially important risks of aspirin withdrawal syndrome. We were not able to clearly assess the reason for aspirin therapy in our patient population, and therefore we chose to universally continue aspirin independent of the clear or unclear reasons for its use.

The patients were queried about the continuation of their aspirin on the morning of their procedure by their attending surgeon. If they had stopped their aspirin on the basis of an erroneous instructions they had received from others (this occurred rarely), then they were given 81 mg of enteric-coated aspirin orally in the preoperative area 1 hour before the induction of anesthesia. After the operation, oral aspirin therapy has been resumed on postoperative day 1 (POD 1) to eliminate interruptions in antiplatelet therapy.

Patients undergoing pancreatoduodenectomy[14] and distal pancreatectomy[15] were managed routinely on our previously published critical pathways, which include the subcutaneous administration of 5,000 units of unfractionated heparin approximately 2 hours before the skin incision, and the routine use of either heparin (5,000 units subcutaneously every 8 hours) or enoxaparin (40 mg subcutaneously every day) postoperatively, starting on the day after the operation (POD 1).

The records for patients undergoing pancreatoduodenectomy, distal pancreatectomy, or total pancreatectomy between October 2005 and February 2012 were queried for perioperative aspirin use. A total of 1,044 patients were identified and were eligible to be included in the analysis. Twenty-seven patients were excluded because of our inability to obtain accurately their perioperative medication usage data. The total number of patients included in the final analysis was 1,017 patients, with 289 patients being aspirin users and 728 patients not using aspirin. This study was approved by the Thomas Jefferson University Institutional Review Board.

Data collection. The patient data were collected in a prospectively maintained, institutional review board–approved pancreatic resection database that included demographics, intraoperative parameters, pathology, postoperative duration of hospital stay, and perioperative complications. A retrospective chart review was performed to obtain detailed perioperative medication use, including use of aspirin, other COX inhibitors, ADP inhibitors, glycoprotein IIb/IIIa inhibitors, vitamin K antagonists, antithrombin III activators, and